Long-term functional patency and cost-effectiveness of arteriovenous fistula creation under regional anaesthesia: a randomised controlled trial

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Abstract

Background

Regional anaesthesia improves short-term blood flow through arteriovenous fistulae (AVF). We previously demonstrated that regional anaesthesia (RA) compared to local anaesthesia (LA) improves primary AVF patency at three months. In this study, we report the effects of anaesthesia on longer-term AVF patency with corresponding cost-benefit analysis.

Methods

We performed an observer-blinded randomised controlled trial at three university hospitals in Glasgow, UK. 126 patients undergoing primary radiocephalic or brachiocephalic AVF creation were randomised to receive RA (brachial plexus block; 0·5% L-bupivacaine and 1·5% lidocaine with epinephrine) or LA (0·5% L-bupivacaine and 1% lidocaine). Primary outcome measures have previously been reported. Primary, functional, and secondary patency at one year, re-interventions, and additional access procedures are reported here. Data were analysed by intention-to-treat. Cost effectiveness analyses were performed. The study was registered with ClinicalTrials.gov (NCT01706354).

Results

At 12 months, both primary patency (50 [79%] vs 37 patients [59%]; OR 2·7 [95% CI 1·6, 3·8], P=0·02) and functional patency (43 [68%] vs 31 patients [49%]; OR 2·1, [95% CI 1·5, 2·7] P=0·008) were higher in the RA cohort. 21 revisional procedures, 53 new AVFs, and 50 TDCs were required in 12 months. RA resulted in net savings of £195·10/patient at one year, and an ICER of approximately £12,900 per QALY over a five-year time horizon. Results were robust following extensive sensitivity and scenario analyses.

Conclusions

Compared to LA, RA significantly improved both primary and functional AVF patency at one year and is cost-effective.

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Introduction

Arteriovenous fistulae (AVF) are the haemodialysis (HD) access modality of choice for patients with end stage renal disease (ESRD)[1] and are associated with lower rates of systemic sepsis and mortality compared to other vascular access options.[2,3] However, the early failure rate is approximately 30%[4-8] and is influenced by pre-operative vessel size, arterial inflow and early post-operative blood flow, all of which can be affected by anaesthetic technique.[9,10]

Regional anaesthesia (RA), such as brachial plexus block (BPB), involves targeted injection of local anaesthetic (LA) to block motor and sensory nerves supplying the operative site. Unlike LA infiltration for AVF creation, RA also blocks sympathetic nerves resulting in vasodilation, improved blood flow and reduced vasospasm both perioperatively and in the early postoperative period.[10,11,12,13] Until recently, there was no evidence that short-term perioperative haemodynamic changes secondary to anaesthesia could improve longer-term fistula patency.[11,14]

We previously demonstrated that medium-term (three month) primary AVF patency rates were higher in patients randomised to RA compared to LA infiltration at the time of radiocephalic (RCF) or brachiocephalic (BCF) fistula creation.[11] However, functional patency rates at this three month time point were lower than anticipated in both cohorts. The effect of anaesthetic technique on longer-term AVF functional patency remains unknown.

Long-term functional patency is the ultimate goal of vascular access surgery, reducing both the need for further vascular access procedures and complications associated with tunnelled dialysis catheters (TDC). If utilising RA improved long-term outcomes it could therefore result in cost-savings, although this would need to be offset against the financial costs of a dedicated anaesthetist, anaesthetic equipment and additional time required.

The purpose of this study was to analyse the clinically relevant outcome of functional AVF patency at one year using follow-up data from our original randomised controlled trial (RCT)

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comparing RA to LA for AVF creation, and to evaluate the cost-effectiveness of each anaesthetic modality.

Methods

Study design and participants

An observer-blinded RCT was performed at three university hospitals in Glasgow, UK (Stobhill Ambulatory Care Hospital, Western Infirmary and Queen Elizabeth University Hospital). The full trial design, methodology and initial (three month) outcomes have been published previously.[11, 15] The trial protocol was approved by West of Scotland Research Ethics Committee 5 (12/WS/0199) (ClinicalTrials.gov Number: NCT01706354) and is available at https://trialsjournal.biomedcentral.com/articles/10.1186/1745-6215-14-263.

A research team member approached eligible patients pre-operatively and assessed for eligibility. Patients were provided with study information before informed, written consent was obtained. The research was undertaken in accordance with the Declaration of Helsinki and was in keeping with the standards set by the International Conference on Harmonisation of Good Clinical Practice.

Adults (aged 18 or older) undergoing primary radiocephalic (RCF) or brachiocephalic (BCF) fistula creation for the purposes of haemodialysis were eligible for inclusion. Patients were excluded if they: were unable or unwilling to provide informed consent; had previous ipsilateral attempts at AVF creation; if the radial or brachial artery was <1.8mm or cephalic vein was <2mm at the wrist or <3mm at the elbow on pre-operative ultrasound (without tourniquet); had an allergy to local anaesthetic; significant peripheral neuropathy or neurological disorder affecting the upper limb; infection at the anaesthetic or surgical site; coagulopathy; or known ipsilateral central vein stenosis (even if treated).

Randomisation and masking

Patients were randomly assigned (1:1; in blocks of eight) using a computer-generated allocation system to receive either RA or LA. Study allocation was by opaque, sealed envelopes as produced by a member of staff independent of the research team. After

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obtaining consent, each patient was assigned a study number and corresponding sealed envelope containing their study allocation. This was opened by the anaesthetist allocated to the theatre list. Due to the nature of the study intervention, neither the anaesthetist, surgeon, nor patient were blinded. The vascular access nurse performing the assessment of study outcomes was blinded to study allocation.

Procedures:

A detailed description of surgical and anaesthetic techniques has previously been published[11,15] and is available at: https://trialsjournal.biomedcentral.com/articles/10.1186/1745-6215-14-263.In brief, a standard end-to-side RCF or BCF was created. Patients in the RA cohort all received an ultrasound guided BPB performed by one of two experienced consultant anaesthetists. The supraclavicular approach was chosen unless there was a contraindication, in which case an axillary block was undertaken. A 1:1 mixture of 0.5% L-bupivacaine and 1.5% lidocaine with epinephrine (1 in 200,000) was injected up to a maximum volume of 40 mL. Patients in the LA infiltration group received infiltration of local anaesthetic into the surgical site by the operating surgeon under sterile conditions using a combination of 0.5% L-bupivacaine and 1% lidocaine injected subcutaneously immediately prior to the commencement of surgery. Maximum dose limits of 2 mg/kg for bupivacaine and 3 mg/kg for lidocaine (7mg/kg with epinephrine) were observed throughout, recognising that these effects are additive.

Clinical outcomes

The primary outcome has been reported previously.[11] Secondary end points reported here include primary, functional and secondary patency at one year. Functional patency was assessed both clinically as an AVF suitable for dialysis and by ultrasound (>6mm diameter, <6mm from skin surface and flow rate >600ml/min[16]). Additional interventions (angioplasty, stenting and surgical revision); alternative vascular access formation and adverse events, including access-related complications (infection, stenosis, thrombosis), were also recorded. Definitions of patency are derived from Sidawy *et al* [17] and are outlined in the Supplementary Appendix.

Statistical analysis

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Results were analysed using SPSS Statistics v22 (Armonk, NY). Data were tested for normality. Assuming normal distribution, student's t-test (2-tailed) was used to compare continuous data, and chi-squared test used to compare categorical data. Mann-Whitney U-tests were used for non-normally distributed data. Logistic regression analysis was carried out to examine the interaction between AVF site (RCF/ BCF) and anaesthesia on primary and functional patency. P<0·05 was considered significant. Results are presented as mean (95% CI), median (IQR), or as a percentage of the total population and odds ratio (OR). Missing data were limited and assumed to be missing at random. If a data point was missing, this case was removed from analysis of the specific variable of interest. A "last-forward" approach was taken towards fistula patency in patients who died. Data were analysed on an intention-to-treat basis. The study was powered according to the primary outcome[11] and no formal power calculation was performed for the secondary endpoints reported in this paper.

Cost-comparison and cost-effectiveness analysis

A probabilistic state-transition (Markov) model was developed, tracking the progression of patients with ESRD across various health states representing alternative vascular access modalities. Nested decision trees captured the pathways associated with the creation and maturation of new AVFs (Figure 1). Transition probabilities were derived from clinical data observed in the RCT across the one-year follow-up (Appendix table S1).

All costs were estimated from the perspective of the National Health Service (NHS) and were converted to 2019/2020 United Kingdom Pound Sterling (GBP/£). A "bottom-up" approach was used to estimate costs associated with each anaesthetic technique including medication, equipment and staff time. Costs were derived from the British National Formulary (BNF);[19] Personal Social Services Research Unit Costs of Health and Social Care 2018;[20] national procurement data;[21] or market prices (Table S2-5) and were validated by clinical experts.

Methodology described by Shechter et al (2017)[22] was applied to derive baseline health utility scores for HD via different access modalities using previously published data.[23,24] As

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such, baseline utility values of 0·767 and 0·677 were assigned to health states "HD via AVF" and "HD via TDC" respectively (Table S6).

Two sets of results were estimated. Firstly, resource utilisation data derived directly from the one-year follow-up of patients in the RCT was employed for cost-comparison analysis. A one-way sensitivity analysis was undertaken (+/-20%) to evaluate the influence of key factors. Secondly, the decision-analytic model described above was used to estimate the relative cost-effectiveness of RA compared to LA across a five-year time horizon. Costs and health benefits were tracked and aggregated, and incremental cost-effectiveness ratios (ICERs) were estimated (expressed in GBP per life-year and per quality-adjusted life-year (QALY)). One-way sensitivity analysis was conducted and structural uncertainty in the model was investigated through a series of scenario analyses. Finally, the joint parameter uncertainty was explored by second order Monte Carlo simulation in which a probabilistic distribution was fitted around each model parameter and 1,000 simulations run, repeatedly sampling different point estimates from these distributions and estimating alternative probabilistic model results. The parameters for the distributions were estimated from available or assumed sample statistics using the method of moments (Appendix Table S6).

Role of the funding source

The funder of the study had no role in study design, data study had no role in study design, data collection, data analysis, data interpretation, or writing of the writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication

Results

Between 6th Feb 2013, and 4th Dec 2015, 163 patients were assessed for eligibility and 126 patients were randomly assigned to LA (n=63) or RA (n=63) (Figure 2). One patient breached protocol having been randomly assigned before vein mapping ultrasound (no suitable vessels identified). 6 patients (4 in the RA cohort and 2 in the LA cohort) died between 3 and 12 months follow-up. Otherwise all patients completed 12-month follow-up on an intention-to-treat basis.

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Patient demographics have been described previously.[11] The groups were similar in terms of age, sex, comorbidities, renal replacement modality and other baseline variables (Table 1). 51 (40%) of 126 patients randomly assigned had a RCF created whilst the remaining 75 (60%) had a BCF creation.

Primary patency at 12 months was higher in the RA group compared to the LA group (50 [79%] vs 37 patients [59%]; OR 2·7 [95% CI 1·6, 3·8], P=0·02) (fragility index=2). Similarly, functional patency at 1 year was higher in the RA cohort (43 [68%] vs 31 patients [49%]; OR 2·1, [95% CI 1·5, 2·7] P<0.01) (fragility index=2) (Table 2).

The observed benefits of RA were more marked in RCF than BCF, although formal interaction tests did not find demonstrate significance (Tables 3 & 4). Primary and functional patency rates at 12 months in RCF were 77% vs.48% (P=0.02) and 78% vs. 48% (P=0.02). No statistical significantly difference in functional patency at 1 year was observed in BCF (76% vs. 63%; P=0.25). Although not significantly different between RA and LA, overall functional patency of BCF was better at 12-months than 3-months (53 [69%] vs 15 patients [20%], P<0·01).

21 revisional procedures were performed in 14 patients (Table 5). 13 patients (93%) successfully achieved functional patency as a result of these interventions. All revisional procedures were performed in BCF. No RCF required intervention. 15 of the 21 revisional procedures (71.4%) were performed in the RA cohort. Conversely more new AVF and temporary dialysis catheters (TDCs) were required in the LA cohort. Additionally, a further 24 AVF (13 RA, 11 LA), which hadn't achieved functional patency by 3 months, subsequently achieved functional patency by 12 months without additional intervention.

7 patients (4 RA, 3 LA) died during the 12-month follow-up period. No death was associated with vascular access complications. There were no complications of anaesthetic administration. One patient (LA) experienced a superficial wound infection. There was one case of line sepsis in the LA cohort (treated with 14 days of intravenous antibiotics). Mean duration of hospital stay for vascular access issues was 2·5 days (range: 1-17) in 12 months.

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High initial staff time costs in the RA cohort were offset by cost-savings of improved AVF maturation (fewer additional new AVF procedures and reduced TDC complications), delivering an overall net cost saving of £195·10 per patient at 1 year (Table 6). Full details of costs associated with anaesthesia, initial AVF surgery, revisions, additional accesses and sensitivity analyses are outlined in the Supplementary Table 3. The incremental cost was most sensitive to the number of alternative accesses (both AVF and TDCs) created but RA remained cost saving in most cases (Supplemental Figure 1).

Base case results demonstrating relative cost-effectiveness of RA compared to LA over a five-year time horizon are summarised in Table 7. Over five years, RA resulted in a cost saving of approximately £2,100 per patient. In the RA cohort, patients spent relatively more time dialysing via AVF and derived an incremental survival and QALY benefit. The ICERs realised in the RA arm compared to the LA arm were approximately £10,300 per LY gained and £12,900 per QALY gained respectively. The robustness of base-case ICER (£/QALY) to variations in a wide range of model parameters and under various scenarios was investigated by one-way sensitivity analysis as outlined in the Supplementary Appendix (Figure 3, Table S7). RA was cost-effective at a £30,000/QALY threshold in all but one case: when the cost of dialysing via AVF was increased by 20%, the ICER picked up to approximately £33,000/QALY. The ICER was not higher than £30,000/QALY in any other case and in several cases RA dominated LA, offering a higher health benefit for a lower cost.

The ongoing costs of HD are a big driver of cost-effectiveness results, with the NHS England cost of “HD via AVF” being paradoxically higher than “HD via TDC”. Excluding these costs resulted in RA dominating LA. The same effect is observed when the time-horizon of the analysis is reduced. The proportion of the cohort that are pre-dialysis at the start of the model also has a substantial impact on results, with RA being particularly cost-effective in patients already on dialysis at the time of initial AVF creation.

Probabilistic sensitivity analysis results show a high probability of RA being cost-effective (89·6% at £30,000/QALY threshold and 76·3% at £20,000/QALY threshold) compared to LA

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(Figure 4). Moreover, the probability of RA to dominate LA is substantial (39·1%), whereas the probability of RA being dominated by LA is virtually zero (0·0%) (Figure 5).

Discussion

These results confirm an enduring superiority of RA over LA in achieving primary and functional AVF patency at 12 months and are, to our knowledge, the first randomised data to demonstrate an anaesthetic technique improving any long-term surgical outcome. The results also prove RA is cost-effective in AVF creation. Our findings serve to address criticisms ascribed to our original RCT,[11] namely poor functional patency rates, particularly in BCF.

The 12 month functional patency rates described here are comparable to those observed in other large vascular access RCTs[8,24,25] and are reflective of the contemporaneous Scottish population.[26] We hypothesised that absence of assisted maturation techniques, co-morbidity and obesity (difficulties cannulating deep AVF, or failing to meet our functional patency criteria of less than 6mm from skin surface) may explain the relatively poor three month functional patency rates previously observed. These follow-up data suggest that, whilst revisional procedures were required in 14 patients, a further 24 AVF developed functional patency between three and 12 months without intervention, simply requiring additional time to mature. This supports the assertion that the early maturation period is key to long-term functional patency, especially amongst RCF where the functional patency rates at 12 months closely mirror primary patency at three months. Our data suggest that, if early patency (assisted by increased blood flow and vasodilatation secondary to RA) is established, it will ultimately be possible to achieve functional patency. This should be considered when determining end-points for future clinical trials.

As with our previous study[11], the beneficial effect of RA was more marked in the small vessels of RCF. Multiple interventions were needed, mainly in the RA cohort, to assist in the maturation of poorly developed fistulae. However, the cost of these interventions was offset against a need for more alternative accesses (de novo AVF and TDCs) in the LA cohort. Due to the relatively small sample size, cost-effectiveness analysis was not performed for

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RCF and BCF as independent subgroups. It follows however that most of the cost savings are likely to be observed in patients undergoing distal fistula creation.

Three smaller randomised trials all demonstrated the beneficial effects of RA in short-term AVF maturation although these have been considered to have a high level of bias with outcomes often limited to surrogate data.[27, 28,29] Two recent meta-analyses also favoured RA[14, 30] but no trial to date has studied the long-term effects of RA. Nevertheless the recent European Vascular Access and European Renal Best Practice guidelines recommend the use of RA for AVF creation[1, 31]. This guidance also states that RA may increase costs or delay the access procedure, which we have now demonstrated not to be the case. The recently commissioned National Institute for Health Research systematic review demonstrated a reduction of AVF failure by 72% with RA concluding that future studies should also include a cost-analysis.[32]

The study population is largely reflective of UK practice, however it's acknowledged that demographic differences exist internationally. For example in the USA there is a larger proportion of obese and diabetic patients (factors known to be associated with adverse AVF outcomes[33]). Similarly, in the USA assisted maturation techniques are commonly used early in the fistula lifespan, in part to address targets imposed by Centres for Medicare & Medicaid Services (CMS) targets aiming to achieve freedom from TDC by 90 days. Recent US analysis suggests rates of secondary AVF interventions as high as 44%[34]. It is therefore difficult to extrapolate our results to this population as only 11% of patients in this study had an intervention to assist maturation, none within the first 90 days.

The study is limited by the lack of original quality of life (QoL) data. Baseline utility scores were extrapolated from other studies of health-related QoL outcomes in HD patients.[23, 24] These studies used KDQOL-SF and SF-36 to measure QoL in dialysis patients. However, to date, there is no validated QoL tool evaluating the impact of either dialysis modality or vascular access specifically. Such a tool is urgently needed for performing future cost-effectiveness analyses of vascular access.

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With these results we demonstrate, for the first time, net cost-savings and long-term cost-effectiveness of RA. The cost-analysis presented reflects UK practice with health economic analysis performed from the perspective of the National Health Service (NHS) and UK Personal and Social Services. It is acknowledged that costs in other healthcare systems will vary with differences in both perioperative care pathways (e.g. availability of block rooms, different anaesthetic agents, availability of trained anaesthetists) and subsequent interventions to provide a functional access for dialysis (e.g. assisted maturation techniques, resource implications of TDC etc.) such that extrapolation of the absolute cost savings demonstrated within a UK setting may be limited. However results appear robust throughout extensive sensitivity and scenario analyses and our model could be adapted to reflect variations in healthcare in an international setting.

Even within our model, the distribution of cost-savings is complex and controversial. The national tariff in England and Wales incentivises AVF use by providing cost-savings to individual dialysis centres for "HD via AVF". However, the overall net costs to the health service, society at large, and therefore to cost-effectiveness analyses, are higher than "HD via TDC". The "costs" of care are not actually higher with AVF, rather the commissioner-to-institution reimbursement is. The decision whether or not to include ongoing HD costs in cost-effectiveness analysis is therefore a matter of debate,[35] given that the more clinically effective an intervention is, the more it will disproportionately impact the costs in favour of the less effective comparator. Similarly the higher overall survival in the RA arm translates to the accruing of relatively higher ongoing costs of HD. These idiosyncrasies lead to underestimating the true cost-effectiveness benefit derived from improving access outcomes. The absence of dialysis-associated costs (such as the need for alternative accesses) limits cost-savings in pre-dialysis patients. These patients should be considered as a separate cohort for future studies of cost-effectiveness. Future studies of cost-effectiveness in vascular access should focus on measurement of long-term *overall* healthcare costs rather than basic maintenance haemodialysis costs and reimbursement fees.

In conclusion, this is the first randomised study of any perioperative intervention to demonstrate enduring improvement in AVF patency at 12 months. We have presented

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mechanistic explanation[11], clinical benefit and evidence of cost-effectiveness. Moreover, this trial demonstrates the value of a multidisciplinary approach to vascular access with motivated surgeons, anaesthetists, nephrologists, access nurses and health economists all contributing. On this basis, we reaffirm our assertion that RA should be used for all *de novo* AVF creation.

Author Contributions

EA was principally responsible for recruitment; collated and analysed the data and wrote the final manuscript. AJ assisted with recruitment and data collection. RK and AM designed the study, wrote the protocol and contributed to the manuscript. LG performed the cost-effectiveness analysis. JK reviewed the design of the study and revision of the final manuscript. MC conceived the study and was the principal surgeon. AM and MS were anaesthetists for the trial. AM had principal responsibility for the study.

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Disclosures

We declare no competing interests.

Data sharing

Data collected for the study will be made available to others on request. The study protocol and informed consent forms will also be made available. Data will be available to researchers who provide a methodologically sound proposal in order to achieve the aims in the approved proposal and reviewers of the manuscript at time of submission. In order to gain access proposals should be directed to the corresponding author. Data will be available for 5 years from the date of the original study.

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Supplementary Material Table of Contents

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Tables

Table 1: Baseline characteristics. Data are presented as n (%) or mean +/- S.D. unless otherwise stated. IHD= ischaemic heart disease; CVA= cerebrovascular accident; HD= haemodialysis; PD= peritoneal dialysis; IQR= interquartile range; Pre-D= pre-dialysis; RA=regional anaesthesia; LA=local anaesthetic
*median (IQR)

	Overall patient population (n=126)	**RA (n=63)**	**LA (n=63)**
Age (years)	60·8+/-14·8	59·5+/-15·3	62·1+/-14·3
Sex (% male)	79 (62·7%)	40 (63·5%)	39 (61·9%)
Primary renal disease			
Diabetes	21 (16·7%)	10 (15·9%)	11 (17·5%)
Multisystem	16 (12·7%)	9 (14·3%)	7 (11·1%)
Interstitial	41 (32·5%)	16 (25·4%)	25 (39·7%)
Glomerulonephritis	24 (19·0%)	15 (23·8%)	9 (14·2%)
Unknown	24 (19·0%)	13 (20·6%)	11 (17·5%)
Co-morbidities			
Diabetes	34 (27·0%)	17 (27·0%)	17 (27·0%)
IHD	48 (38·1%)	22 (34·9%)	26 (41·2%)
CVA	9 (7·1%)	3 (4·8%)	6 (9·5%)
Hypertension	93 (73·8%)	40 (68·3%)	53 (84·1%)
Obesity (BMI <30)	41 (32·5%)	22 (34·9%)	19 (30·2%)
Medications			
Antihypertensives (number)*	2 (1,4)	2 (1,4)	2 (1,4)
Aspirin	85 (67·4%)	42 (66·7%)	43 (68·3%)
Clopidogrel	29 (23·0%)	13 (20·6%)	16 (25·4%)
Statin	73 (57·9%)	38 (60·3%)	35 (55·6%)
RRT modality at time of randomization			
HD	63 (50%)	30 (47·6%)	33 (52·4%)
Pre-dialysis	63 (50%)	33 (52·4%)	30 (47·6%)
Site of AVF			
RCF	51 (40·5%)	26 (41·2%)	25 (39·7%)
BCF	75 (59·5%)	37 (58·7%)	38 (60·3%)
Surgeon			
1	35 (27·8%)	16 (25·4%)	19 (30·2%)
2	23 (18·3%)	13 (20·6%)	10 (15·9%)
3	16 (12·7%)	8 (12·7%)	8 (12·7%)
4	16 (12·7%)	8 (12·7%)	8 (12·7%)
5	14 (11·1%)	8 (12·7%)	6 (9·5%)
Others	22 (17 ·4%)	10 (15·9%)	12 (19·0%)
Anaesthetist			
1		36 (57·1%)	
2		27(42·9%)	

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Table 2: Patency rates of AVF (primary, secondary and functional patencies at 3 and 12 months). Numbers presented are total number of patients (percentage [95% CI]). AVF=arteriovenous fistula; BCF=brachiocephalic fistula; RCF=radiocephalic fistula; RA=regional anaesthesia; LA=local anaesthetic

	Overall patient population (n=126)	**RA (n=63)**	**LA (n=63)**	**P-value**
ALL AVF				
Primary patency at 3 months	92 (73%) [65%, 80%]	53 (84%) [73%,91%]	39 (62%) [49%,72%]	<0·01
Functional patency at 3 months	44 (35%) [27%, 44%]	26 (41%) [30%, 54%]	18 (29%) [19%, 41%]	0·15
Secondary patency at 3 months	92 (73%) [65%, 80%]	53 (84%) [73%,91%]	39 (62%) [49%,72%]	<0·01
Primary patency at 1 year	87 (69%) [64%,76%]	50 (79%) [72%, 86%]	37 (59%) [54%, 63%]	0·02
Functional patency at 1 year	74 (59%) [62%, 72%]	43 (68%) [7%, 82%}	31 (49%) [52%, 62%]	<0.01
Secondary patency at 1 year	71 (56%) [50%, 62%]	40 (62%) [55%, 69%]	31 (49%) [44%, 55%]	0·04
RCF (n=51)				
Primary patency at 3 months	32 (63%) [50%, 76%]	20 (77%) [65%, 87%]	12 (48%) [35%, 61%]	0·03
Functional patency at 3 months	29 (57%) [44%,71%]	19 (73%) [56%, 89%]	10 (40%) [23%, 59%]	0·02
Secondary patency at 3 months	32 (63%) [50%, 76%]	20 (77%) [65%, 87%]	12 (48%) [35%, 61%]	0·03
Primary patency at 1 year	32 (63%) [50%, 76%]	20 (77%) [65%, 87%]	12 (48%) [35%, 61%]	0·02
Functional patency at 1 year	33 (65%) [49%, 75%}	21(78%) [66%, 88%]	12 (48%) [35%, 61%]	0·02
Secondary patency at 1 year	31 (61%) [49%, 73%]	19 (73%) [65%, 81%]	12 (48%) [35%, 61%]	0·04
BCF (n=75)				
Primary patency at 3 months	60 (80%) [66%,85%]	33 (89%) [72%,95%]	27 (71%) [55%, 73%]	0·05
Functional patency at 3 months	15 (20%) [12%, 29%]	7 (19%) [9%, 34%]	8 (21%) [11%, 37%]	0·95
Secondary patency at 3 months	60 (80%) [66%,85%]	33 (89%) [72%,95%]	27 (71%) [55%, 73%]	0·05
Primary patency at 1 year	55 (73%) [67%, 81%]	30 (81%) [72%, 90%]	25 (68%) [60%, 76%]	0·36
Functional patency at 1 year	53 (69%) [63%, 75%]	29 (76%) [69%, 83%]	24 (63%) [56%, 71%]	0·25
Secondary patency at 1 year	41(55%) [51%, 58%]	22 (56%) [51%, 61%]	19 (50%) [44%, 56%]	0.46

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Table 3: Logistic regression analysis examining the interaction between anaesthetic type and AVF site on primary patency at 12 months. RCF=radiocephalic; BCF=brachiocephalic; RA=regional anaesthesia; LA= local anaesthesia. *Reference: RCF; ** Reference RA

	Beta	**Standard error**	**Wald statistic**	**P-value**	**Exp (B)**	**95% CI**
Intercept	0.70	0.68	1.04	0.31		
AVF site (RCF/ BCF)*	-0.66	0.40	2.70	0.10	0.52	0.23, 1.14
Anaesthetic type (RA/ LA)**	-1.04	0.41	6.41	0.01	0.35	0.16, 0.80

Table 4: Logistic regression analysis examining the interaction between anaesthetic type and AVF site on functional patency at 12 months. RCF=radiocephalic; BCF=brachiocephalic; RA=regional anaesthesia; LA= local anaesthesia.*Reference: RCF; ** Reference RA

	Beta	**Standard error**	**Wald statistic**	**P-value**	**Exp (B)**	**95% CI**
Intercept	0.40	0.69	0.35	0.55		
AVF site (RCF/ BCF)*	-0.43	0.40	1.2	0.28	0.65	0.30, 1.40
Anaesthetic type (RA/ LA)**	-1.08	0.40	7.1	0.007	0.34	0.50, 0.75

Table 5: Number of additional procedures first year. *denotes an intervention for failure to mature/ assisted functional patency. Number of patients is reflected in brackets ()

	RA	LA
Superficialisation/ transposition	4 (4)	3 (2)
Collateral/ branch ligation	2 (2)	
Superficialisation and collateral ligation		1 (1)
Revision of arterial inflow and collateral ligation	1 (1)	
Distal revascularisation and interval ligation	1 (1)	
Proximalisation	1 (1)	
Radiological declot and angioplasty	1 (1)	
Angioplasty (outflow)	4 (3)	1 (1)
Angioplasty and central venous stenting	2 (2)	
New AVF	20 (18)	33 (27)
AVG	3 (3)	3 (3)
Tunnelled dialysis catheter (TDC)	21 (18)	29 (20)
Temporary dialysis catheter	4 (3)	4 (4)

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Table 6: Breakdown of costs per patient in the RA and LA arms at 1-year follow-up

	LA	RA
Anaesthesia component	£2·61	£87·43
Medicines	*£2·44*	*£13·33*
Equipment/consumables	*£0·17*	*£21·51*
Staff time	*negligible*	*£52·60*
AVF surgery	£2,095·00	£2,095·00
Revision procedures	£97·37	£343·84
Additional AVFs	£1,097·38	£665·08
TDC insertion	£341·10	£247·00
Total cost	£3,633·45	£3,438·35
Incremental cost		**-£195·10**

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Table 7: Base case results cost-effectiveness analysis (per patient)

	LA	RA	Incremental
Costs			
Anaesthesia	£6·24	£140·99	£134·75
AVF surgery	£5,011·13	£3,378·34	-£1,632·79
Revisions	£46·13	£167·03	£120·89
TDC costs	£729·86	£397·14	-£332·72
Infection costs	£4,485·06	£3,021·97	-£1,463·09
HD costs	£75,833·72	£81,111·14	£5,277·42
Total	£86,112·14	£88,216·60	**£2,104·46**
Health benefits			
HD via AVF (months)	29·3	38·1	8·7
HD via TDC (months)	11·0	4·7	-6·3
Infection episodes	0·65	0·43	-0.22
Life-years (LYs)	3·842	4·047	0·205
QALYs	2·673	2·836	**0·163**
ICER (£/LY)			£10,256·82
ICER (£/QALY)			**£12,898·87**

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